ASBESTOS EXPOSURE, CIGARETTE SMOKING AND DEATH RATES*

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Before 1966, there was evidence from a number of studies conducted in several different countries that people with a history of occupational exposure to asbestos dust are at risk of developing asbestosis and mesothelioma and at very high risk of lung cancer.[1-4] There was also evidence that mesothelioma or lung cancer resulting from asbestos exposure does not usually appear until many years after initial exposure.[5] Little more was known about the sometimes fatal effects of exposure to asbestos dust although there was some evidence that it increases the risk of cancer of the digestive tract.[3]

This investigation was started in 1966 primarily to obtain information on the combined effects of cigarette smoking and exposure to asbestos dust in respect to death from lung cancer and chronic noninfectious pulmonary diseases; to obtain further evidence concerning cancer other than mesothelioma and lung cancer; and to obtain information on the degree to which occupational exposure to asbestos dust increases total death rates from all causes combined. Some of the early findings have been published.[6,7]

In any study of the effects of exposure to asbestos dust it is necessary to have information on two groups of people: an exposed group and a nonexposed group usually called the "control group." Obviously, the two groups should be as alike as possible except in respect to asbestos exposure. In mortality studies, the total population is often used as the control group; and age–sex specific death rates as usually reported for the total population are compared with the age–sex specific death rates of asbestos workers. When this is done (and we have done it) it is only because of lack of availability of a more suitable control group. For this investigation, we could not use the total population as the only control group for the reason that we needed to have information on the age-specific death rates of men with each of various types of smoking histories; and such information is not available for the total population. Therefore, we had to obtain a more suitable control group described later.

The Exposed Group

This investigation was made possible by the splendid cooperation of the International Association of Heat and Frost Insulators and Asbestos Workers that has about

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120 locals in the United States and Canada. Until recently, most of the material handled by these insulation workers contained asbestos. Therefore, we will refer to all of the members as asbestos workers. The union supplied us with their complete membership list and in 1966 we wrote to each member requesting him to complete a questionnaire containing a number of questions including those on his smoking habits and his use (or nonuse) of protective masks. Date of birth and date of entry into the trade were ascertained from union records.

All of these men have been traced through December 31, 1976 and copies of the death certificates of those who died have been obtained. Since cause of death recorded on a death certificate is not always accurate, we wrote to the doctor who signed the certificate requesting further details on diagnosis as well as to the hospitals in which treatment may have been given, requesting them to lend us histologic slides and/or x-ray films. Treating physicians, pathologists, hospitals were extremely cooperative in this matter.

Some of the men on the 1966 membership list died before January 1, 1967 leaving 17,800 alive at that date (TABLE 1). Altogether 2271 died in the ten–year period

TABLE 1

NUMBER OF MEN, MAN–YEARS OF OBSERVATION, OBSERVED DEATHS AND AVERAGE AGE DURING OBSERVATION, TOTAL, AND UP TO AND MORE THAN 20 YEARS FROM ONSET OF ASBESTOS EXPOSURE IN A COHORT OF ASBESTOS INSULATION WORKERS IN THE UNITED STATES AND CANADA, JANUARY 1, 1967–DECEMBER 31, 1976

		Asbestos Exposure*	
	Total	<20 Years	20+ Years
Number of men	17,800	12,683	12,051
Number of man–years	166,853	89,462	77,391
Number of deaths	2,271	325	1,946
Average age during observation	44.4	36.3	53.8

*As of January 1, 1967, 5117 men had reached the 20+ year point from onset of occupational exposure to asbestos dust. An additional 6934 men reached that point at some time between January 1, 1967 and December 31, 1976.

January 1, 1967—December 31, 1976; the number of man–years of observation totaled 166,853; and the average age of the men during the ten–year period was 44.4. Of the 17,800 men, 5117 had entered the trade 20+ years prior to January 1, 1967; and 1573 of these died before January 1, 1977. Between January 1, 1967 and December 31, 1976, another 6934 men passed the 20–year point since entering the trade; and 373 of these died in the interval between the time they passed the 20–year point and December 31, 1976. Thus a total of 5117 + 6934 = 12,051 men had either reached the 20–year point prior to January 1, 1967 or reached that point before January 1, 1977. The number of man–years of experience past the 20–year point totaled 77,391; the average age during observation was 53.8; and there were 1946 deaths. This report is confined to the 77,391 man–years of observation and the 1946 deaths just mentioned.

THE CONTROL GROUP

Starting on October 1, 1959, 468,688 men and 610,206 women were enrolled in a long term prospective epidemiological study by volunteer workers of the American Cancer Society in 1121 counties in 25 states.[8] All of them were over 30 years old at

that time and most of them were over 40. Upon enrollment, each subject answered a detailed questionnaire; and most of the survivors answered repeat questionnaires distributed in 1961, 1963, and 1965. During that time, death certificates were obtained on those who died; and when cancer was mentioned on a death certificate, the doctor who signed the certificate was requested to supply additional information on the cause of death and the basis of the diagnosis. Follow–up was then discontinued for six years.

Tracing of the subjects was resumed on October 1, 1971 and was continued through September 30, 1972. (We are still following subjects who were very old at that time). One of the major reasons we resumed the tracing was to obtain a suitable control group for the present investigation. Because of the extremely large number of deaths after 1965, it was not feasible for us to request doctors to supply us with additional information on cause of death.

The selection of the subjects was such that persons at the bottom of the social scale were almost entirely excluded (e.g., impoverished migrant workers, illiterates, illegal immigrants, prison inmates, etc.). Persons in these categories are not members of the asbestos insulation workers union; but they are included in the mortality statistics of the United States, and their death rates are very high. On the other hand, unlike the asbestos workers, a large proportion of the male subjects was employed in sedentary occupations involving little or no physical exertion; and lack of exercise is associated with increased risk of coronary heart disease—the leading cause of death among males in the United States. In contrast, men lacking a college education and with a history of occupational exposure to dust, fumes, gases, chemicals, or radiation are most likely to be in occupations involving physical exertion; and in this respect they are similar to members of the asbestos insulation workers union. Some such exposures increase the risk of cancer or pulmonary disease. Most of the members of the asbestos insulation workers union were white and virtually none of them were farmers.

For these reasons we selected as a control group for this investigation all of the male subjects who met the following specifications: white, not a farmer, no more than a high school education, a history of occupational exposure to dust, fumes, vapors, gases, chemicals or radiation and alive as of January 1, 1967 and traced thereafter. There were 73,763 such subjects. They were classified according to their smoking histories and the age–specific death rates of each such class was computed.

There was a problem. Death rates in the control group were known for the period January 1, 1967 through September 30, 1972 while members of the asbestos insulation workers union were traced during the period January 1, 1967–December 31, 1976. According to official mortality statistics, death rates of the general population of the United States changed somewhat during the second five–year period January 1, 1972–December 31, 1976 compared with the first, January 1, 1967–December 31, 1971, increasing for some diseases and declining for other diseases. Under the assumption that these changes probably also applied to the control group, the death rates of the control group were extrapolated to take this into account. The principal effect of the extrapolation was to increase the death rates from lung cancer and decrease the death rates from heart disease during the last five years as compared with the first five years.

CAUSES OF DEATH

Because of the pressure to fill out a death certificate promptly so that the body may be moved, what is recorded on the certificate is not always the best available information on cause of death. For example, in the absence of the patient's physician, the certificate may be signed by a doctor who knows less about the case; or an autopsy

may indicate that the tentative diagnosis of cause of death was incorrect; or a review of the evidence may indicate for example, that the patient died of peritoneal mesothelioma involving the pancreas rather than having died of primary carcinoma of the pancreas. Fortunately, we were able to obtain additional medical information on almost all of the asbestos workers who died; and in many instances histologic sections or x-ray films were loaned to us for further review.

The first column of figures in TABLE 2 shows the 1946 deaths classified by underlying cause of death according to what was written on the death certificates, following as nearly as possible the coding rules used by the United States National Center for Health Statistics. The second column shows these same deaths classified according to the best available medical information, including, in many instances,

TABLE 2

DEATHS OCCURRING 20+ YEARS AFTER ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST. CAUSE OF DEATH CODED IN TWO DIFFERENT WAYS

Underlying Cause of Death	Based on Death Certificates Only (DC)	Based on Best Evidence Available (BE)	Difference (BE)–(DC)
All Causes	1,946	1,946	—
Cancer, all sites	845	912	+67
Lung	397	450	+53
Pleural mesothelioma	23	61	+38
Peritoneal mesothelioma	24	109	+85
Mesothelioma not specified above	54	0	−54
Larynx, buccal and pharynx	21	27	+6
Esophagus	17	17	0
Kidney	15	16	+1
Colon–rectum	54	55	+1
Stomach	18	21	+3
Prostate	24	26	+2
Bladder	7	9	+2
Pancreas	46	21	−25
Other specified sites	110	83	−27
Primary site unknown	35	17	−18
Noninfectious pulmonary diseases, total	177	204	+27
Asbestosis	76	160	+84
Cardiovascular diseases	638	566	−72
Other and unspecified causes	286	264	−22
Subtotal—all causes except cardiovascular diseases	1,308	1,380	+72

review of histologic sections by pathologists with a special interest in mesothelioma and review of x-ray films by physicians with a special interest in asbestosis. In some instances, two or more pathologic conditions are present in such degrees that any one of them alone or the combined effects might have been responsible for death. Our procedure is to code up to three such conditions (i.e., diseases or injuries). Following international custom, we designate one of these as the underlying cause of death; but this is sometimes a highly arbitrary decision. The third column of figures in TABLE 2 shows the difference between the first column, DC (death certificate), and the second column, BE (best evidence).

There were major discrepancies in the comparative figures. According to death

certificates 845 deaths were due to cancer, while according to the best evidence available 912 deaths were due to cancer, a difference of 67 deaths. On the other hand, according to DC, 638 deaths were due to cardiovascular diseases (including stroke) while according to BE only 566 deaths were due to cardiovascular diseases, a difference of 72 in the opposite direction.

Cancer of the pancreas accounted for 46 deaths (DC) or 21 deaths (BE). The best available medical information and review of histologic sections indicated that of the 46 deaths ascribed to primary cancer of the pancreas according to the death certificates, 15 were actually due to peritoneal mesothelioma, 6 were due to cancer of some other specified primary site and five to unknown primary site. One death attributed to myocardial infarction (DC) was probably due to primary cancer of the pancreas.

Cancer of other specified sites accounted for 110 deaths (DC) or 83 (BE) a difference of 27. Cancer in which the primary site was unknown was assigned 35 deaths (DC) or 17 deaths (BE). Additional medical evidence (sometimes from an autopsy) accounted for this difference.

Mesothelioma accounted for 101 deaths (DC) or 170 deaths (BE), a difference of 69. Most of the extra 69 deaths had been recorded on the death certificate as due to cancer of some other primary site or "cancer, primary site unknown."

The category labeled "noninfectious pulmonary diseases" includes chronic bronchitis, emphysema, pulmonary fibrosis, other nonspecific pulmonary diseases, and pneumoconiosis including asbestosis. This group of diseases caused 177 deaths (DC) or 204 deaths (BE) a difference of 27. The subcategory, asbestosis was termed the underlying cause of death for 76 (DC) or 160 (BE) of these deaths.

OBSERVED VS. EXPECTED NUMBER OF DEATHS

TABLES 3 and 4 show the 1946 observed deaths classified by cause of death in the two different ways previously discussed: from death certificates (DC) and according to the best evidence available (BE). Two different sets of expected numbers of deaths are shown: the expected number based on the age and smoking history specific death rates of men in the control group; and the expected number based upon the age–specific death rates of all white males in the United States as reported by the National Center for Health Statistics for the period 1967–1976. The age standardization was by five–year age groups in each of two five–year intervals of time (1967–1971 and 1972–1976). Thus altogether four sets of comparisons between observed and expected numbers of deaths are shown. This was done because there may be differences of opinion as to which set is preferable. In this analysis, in most instances, we prefer comparisons of the expected deaths based on the control group rates with the observed deaths classified according to the death certificates. Our reasons are: the control group subjects were similar to the asbestos workers in respect to education and in respect to general type of work (i.e. work involving physical exercise and a history of exposure to dust etc.), smoking habits were taken into consideration, and although death certificates are not always accurate, when two groups are compared it is highly desirable that information on the causes of death come from the same source. However, the set of comparisons just mentioned leads to overestimation of the degree of association between exposure to asbestos and death from cancer of the pancreas while it underestimates the impact of mesothelioma and asbestosis. For these diseases, we prefer the comparisons where cause of death was classified according to the best evidence available (BE).

Two indices of association are shown: the mortality difference which is the observed number of deaths minus the expected number of deaths, and the mortality

ratio which is the observed number of deaths divided by the expected number of deaths.

The general findings are shown in TABLE 3. For total deaths (disregarding cause of death) the mortality ratios were 1.70 (control group) and 1.41 (U.S. white males) and the mortality differences were +798.0 and +570.0 respectively. For cancer of all sites combined, the mortality ratios ranged from 3.05 (U.S. white males, DC) to 3.52 (control group, BE) and the mortality differences ranged from +567.9 to +653.0. Thus, according to every comparison, total death rates and death rates from cancer were elevated in the asbestos workers.

The expected number of deaths from noninfectious pulmonary diseases was higher for the control group (68.2) than for U.S. white males (53.8). This is not surprising since men in the control group had a history of occupational exposure to dust, fumes, vapors, etc. The mortality ratios ranged from 2.60 (control group, DC) to 3.79 (U.S. white males, BE) and the mortality difference ranged from +108.8 to +150.2. Asbestosis clearly accounted for these mortality differences. However, it seems likely that many of these deaths were due to the combined effects of asbestosis and damage to the lung parenchyma resulting from cigarette smoking. Evidence on this will be shown later in this paper.

In contrast, the expected numbers of deaths from cardiovascular diseases were lower for the control group (660.1) than for U.S. white males (752.7). We do not know the reason for this, but it may have been due to the fact that men in the control group had a history of occupational exposures usually involving physical exercise (in contrast to clerical work). The mortality ratios ranged from .75 (U.S. white males, BE) to .97 (control group, DC) and the mortality differences ranged from −22.1 to −186.7.

Considering all causes of death except cardiovascular disease, the mortality ratios ranged from 2.10 (U.S. white males, DC) to 2.83 (control group, BE).

TABLE 4 shows the findings for cancer of several different sites. For lung cancer, the mortality ratios ranged from 4.24 (U.S. white males, DC) to 5.51 (control group, BE) and the mortality differences ranged from +303.3 to +368.3. Thus, no matter which of the various comparisons is considered to be the most reliable, it is clearly apparent that death rates from lung cancer were greatly increased in this group of asbestos workers—enough so as to cause a significant decrease in their life expectancy. From the standpoint of longevity, this was the most important effect of exposure to asbestos dust in a group of workers, the majority of whom had a history of cigarette smoking.

Death rates from mesothelioma are not available for either the control group or U.S. white males; but they are presumably extremely low in these two groups, so the expected numbers of deaths from mesothelioma were probably less than 0.1. Consequently the mortality ratios must be extremely high. The mortality difference ranged from a trifle less than 101 to a trifle less than 170. The former figure is certainly an underestimate while the latter figure, which is based upon histologic evidence as well as other evidence, is probably very close to correct. According to this evidence, 61 of the asbestos workers died of pleural mesothelioma and 109 died of peritoneal mesothelioma.

Cancer originating in the larynx, pharynx or buccal cavity is more readily diagnosed than cancer of some other sites; and in a previous study, deaths from cancer of these sites were generally reported correctly on death certificates. Therefore, we were surprised that according to the death certificates only 21 of the asbestos workers died of cancer of these sites, while according to the best available evidence 27 died of these cancers. The mortality ratios ranged from 1.60 (U.S. while males, DC) to 3.60 (control group, BE). Two of the mortality differences are statistically significant at the level of $p < .05$; the other two are not.

TABLE 3

OBSERVED AND EXPECTED NUMBER OF DEATHS OCCURRING 20+ YEARS AFTER ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Underlying Cause of Death	Observed Deaths		Control Group†			U.S. White Males		
	From‡	Total	Expected Deaths	Observed Minus Expected	Ratio Observed/ Expected	Expected Deaths	Observed Minus Expected	Ratio Observed/ Expected
All causes	—	1946	1148.0	+798.0	1.70	1376.0	+570.0	1.41
Cancer	DC	845	259.0	+586.0	3.26	277.1	+567.9	3.05
	BE	912		+653.0	3.52		+634.9	3.29
Cardiovascular	DC	638	660.1	−22.1	0.97	752.7	−114.7	0.85
	BE	566		−94.1	0.86		−186.7	0.75
Noninfectious Pulmonary (total)	DC	177	68.2	+108.8	2.60	53.8	+123.2	3.29
	BE	204		+135.8	2.99		+150.2	3.79
Asbestosis	DC	76	*	+76.0	—	*	+76.0	—
	BE	160		+160.0	—		+160.0	—
All other causes	DC	286	160.8	+125.2	1.78	292.3	−6.3	0.98
	BE	264		+103.2	1.64		−28.3	0.90
Subtotal—all causes exc. cardiovascular	DC	1308	487.9	+820.1	2.68	623.3	+684.7	2.10
	BE	1380		+892.1	2.83		+756.7	2.21

*Control group and U.S. death rates not available but these have been rare causes of death in the general population.
†*Like men in American Cancer Society prospective study* (see text).
‡DC means cause of death according to death certificate information. BE means cause of death according to best evidence available.

TABLE 4

OBSERVED AND EXPECTED NUMBER OF CANCER DEATHS OCCURRING 20+ YEARS AFTER ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Underlying Cause of Death (Cancers)	Observed Deaths From‡	Observed Deaths Total	Control Group† Expected Deaths	Control Group† Observed Minus Expected	Control Group† Ratio Observed Expected	U.S. White Males Expected Deaths	U.S. White Males Observed Minus Expected	U.S. White Males Ratio Observed Expected
Lung	DC	397	81.7	315.3	4.86	93.7	303.3	4.24
	BE	450		368.3	5.51		356.3	4.80
Mesothelioma	DC	101	*	101.0	—	*	101.0	—
	BE	170		170.0	—		170.0	—
Larynx, buccal and pharynx	DC	21	7.5	13.5	2.80	13.1	7.9	1.60
	BE	27		19.5	3.60		13.9	2.05
Esophagus	DC	17	5.1	11.9	3.34	6.5	10.5	2.64
	BE	17		11.9	3.34		10.5	2.64
Kidney	DC	15	8.5	6.5	1.76	7.0	8.0	2.15
	BE	16		7.5	1.88		9.0	2.30
Colon–rectum	DC	54	30.5	23.5	1.77	34.1	19.9	1.59
	BE	55		24.5	1.81		20.9	1.62
Stomach	DC	18	12.5	5.5	1.44	12.7	5.3	1.42
	BE	21		8.5	1.68		8.3	1.65
Prostate	DC	24	18.3	5.7	1.31	19.7	4.3	1.21
	BE	26		7.7	1.42		6.3	1.32
Bladder	DC	7	6.7	0.3	1.04	8.6	−1.6	0.82
	BE	9		2.3	1.34		0.4	1.05
Pancreas	DC	46	16.0	30.0	2.87	15.5	30.5	2.96
	BE	21		5.0	1.31		5.5	1.35
Other and unspecified cancers	DC	145	72.1	72.9	2.01	56.3	78.7	2.19
	BE	100		27.9	1.39		33.7	1.51

*Control group and U.S. death rates not available but these have been rare causes of death in the general population.
†Like men in American Cancer Society prospective study (see text).
‡DC means cause of death according to death certificate information. BE means cause of death according to best evidence available.

For cancer of the esophagus, the mortality ratios ranged from 2.64 to 3.34. The mortality differences ranged from +10.5 to +11.9 and are statistically significant. Without much doubt, exposure to asbestos dust increased the risk of this disease in a group of men, the great majority of whom smoked cigarettes, cigars or pipes.

Colon–rectum cancer was in third place (after lung cancer and mesothelioma) as a cause of cancer death among the asbestos workers. The mortality ratios ranged from 1.59 to 1.81. The mortality differences ranged from +19.9 to +24.5 and are statistically significant ($p < .05$).

For kidney cancer, the mortality ratios ranged from 1.76 (control group, DC) to 2.30 (U.S. white males, BE) and the mortality differences ranged from +6.5 to +9.0. Two of the mortality differences are statistically significant; the other two are not.

Death rates from stomach cancer have been declining rapidly in the United States and only 18 (DC) or 21 (BE) of the asbestos workers died of this disease. The mortality ratios ranged from 1.42 to 1.68. The mortality differences ranged from +5.3 to +8.5 and are not statistically significant ($p > .05$).

Mortality ratios for cancer of the prostate ranged from 1.21 (U.S. white males, DC) to 1.42 (control group, BE). The mortality differences are not statistically significant.

Very few of the asbestos workers died of bladder cancer and there is no indication that exposure to asbestos dust increases the risk of this disease.

The figures for cancer of the pancreas are interesting because so many of the deaths attributed to this disease on death certificates were actually due to mesothelioma. If the death certificate were to be believed, then it would appear that exposure to asbestos dust greatly increases the risk of cancer of the pancreas. Better evidence suggests that death rates from cancer of the pancreas may be slightly elevated in asbestos workers, but this is far from certain.

For cancer of all other sites combined (including cancer of unknown primary sites) the mortality ratios ranged from 1.39 (control group, BE) to 2.19 (U.S. white males, DC). The mortality differences ranged from +27.9 to +78.7 and are statistically significant.

SMOKING HABITS

TABLE 5 shows the age distribution of the asbestos workers as of January 1, 1967 and the smoking habits of those who answered the questionnaire in late 1966. It is confined to the 12,051 men who by January 1, 1967 had passed the 20-year point since entering the trade or who passed the point before January 1, 1977. Of the 8220 men who answered the questionnaire, 891 (11%) said that they had never smoked regularly; 488 (6%) had a history of pipe or cigar smoking but never smoked cigarettes regularly and; 6841 (83%) were either current or ex-cigarette smokers. Some of the cigarette smokers also smoked pipes or cigars or had done so in the past.

Our first question related to the degree to which cigarette smoking increased the death rates of the asbestos workers.[9] This is shown in TABLES 6A and 6B for all causes of death and for lung cancer identified as such from the best available medical evidence (BE) (the preferred classification here because all comparisons are within the asbestos workers group). The asbestos workers were first divided into five groups according to smoking habits: 1) smoked 20+ cigarettes a day; 2) smoked cigarettes regularly but < 20 a day; 3) history of regular pipe or cigar smoking but never smoked cigarettes regularly; 4) never smoked regularly; and 5) smoking habits unknown. The 20+ a day and the < 20 a day cigarette smokers are each subdivided into four groups: "current" meaning that they were smoking cigarettes regularly in 1966; ex-cigarette

TABLE 5

NUMBER OF STUDY GROUP MEN WHO ATTAINED AT LEAST 20 YEARS FROM ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST AT SOME TIME JANUARY 1, 1967–DECEMBER 31, 1976, BY AGE JANUARY 1, 1967, AND BY SMOKING HISTORY AS OF 1966

		History of Smoking (Number of Men)							
Age as of Jan. 1, 1967	Total in Age Group	Cigarettes*	Current Cigarettes 20+/day	Current Cigarettes <20/day	Ex–Cigarettes 20+/day	Ex–Cigarettes <20/day	Never Smoked Regularly	Pipe/Cigar Only	Unknown History
Total	12,051	6,841	3,708	764	1,823	378	891	488	3,831
25–29	339	174	105	29	31	9	27	6	132
30–34	1,662	844	531	100	160	43	142	66	610
35–39	2,610	1,423	863	161	313	65	198	84	905
40–44	2,151	1,336	818	114	329	58	143	69	603
45–49	1,526	923	487	94	265	49	107	61	435
50–54	1,250	792	398	74	253	44	84	46	328
55–59	960	558	248	70	193	33	65	40	297
60–64	693	388	132	63	134	35	50	44	211
65–69	413	203	75	27	74	16	33	31	146
70–74	255	108	28	15	42	15	29	29	89
75–79	111	60	17	12	18	6	5	5	41
80–84	52	19	4	4	5	4	3	5	25
85+	29	13	2	1	6	1	5	2	9

*Includes the cigarette smokers who did not specify the number smoked per day.

TABLE 6A

OBSERVED AND EXPECTED NUMBER OF DEATHS OCCURRING 20+ YEARS AFTER ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST BY SMOKING HISTORY. EXPECTED DEATHS ARE BASED ON AGE-SPECIFIC DEATH RATES OF ALL OF THE ASBESTOS WORKERS

	All Causes of Death		Lung Cancer (BE)†	
Smoking History	Observed Deaths	Expected Deaths	Observed Deaths	Expected Deaths
Total*	1946	1946.0	450	450.0
20+ cigarettes/day				
Current	565	481.3	171	116.8
Ex, <5 yrs.	166	137.5	54	33.3
Ex, 5–9 yrs.	61	69.6	10	17.1
Ex, 10+ yrs.	112	136.5	15	31.4
<20 cigarettes/day				
Current	143	127.6	38	29.5
Ex, <5 yrs.	22	20.0	5	4.8
Ex, 5–9 yrs.	10	11.5	1	2.5
Ex, 10+ yrs.	31	43.6	5	9.8
Pipe/cigar only	86	112.5	3	24.2
Never smoked regularly	94	158.2	5	35.5
Unknown	614	587.6	136	132.6

TABLE 6B

MORTALITY RATIOS OF OBSERVED AND EXPECTED NUMBER OF DEATHS PRESENTED IN TABLE 6A RELATIVE TO TOTAL MEN AND TO THE MORTALITY RATIOS FOR MEN WHO NEVER SMOKED REGULARLY (NSR)

	All Causes of Death		Lung Cancer (BE)†	
Smoking History	Ratio Observed/ Expected	Ratio to NSR	Ratio Observed/ Expected	Ratio to NSR
Total*	1.00	1.68	1.00	7.10
20+ cigarettes/day				
Current	1.17	1.98	1.46	10.40
Ex, <5 yrs.	1.21	2.03	1.62	11.51
Ex, 5–9 yrs.	0.88	1.48	0.58	4.15
Ex, 10+ yrs.	0.82	1.38	0.48	3.39
<20 cigarettes/day				
Current	1.12	1.89	1.29	9.15
Ex, <5 yrs.	1.10	1.85	1.04	7.40
Ex, 5–9 yrs.	0.87	1.46	0.40	2.84
Ex, 10+ yrs.	0.71	1.20	0.51	3.62
Pipe/cigar only	0.76	1.29	0.12	0.88
Never smoked regularly	0.59	1.00	0.14	1.00
Unknown	1.04	1.76	1.03	7.28

*In addition to the smoking groups shown, the total includes the cigarette smokers who did not specify the number smoked per day, or the length of time stopped if an ex-smoker.

†Died of lung cancer according to the best evidence available.

smokers who had given up the habit for <5 years; ex-cigarette smokers who had given up the habit for 5 to 9 years; and ex-cigarette smokers who had given up the habit for 10+ years.

TABLE 6A shows the observed and expected number of deaths in each smoking category. The expected number for each particular category was calculated by applying the age-specific death rates of all the asbestos workers (regardless of smoking history) to the age-specific man-years of exposure to risk for that particular smoking category. TABLE 6B, which is based upon TABLE 6A, shows two different ratios: the mortality ratio calculated by dividing the observed number of deaths by the expected number of deaths (by definition, the mortality ratio for all of the subjects is 1.00), and the ratio relative to never smoked regularly, NSR, which is the mortality ratio for each smoking category divided by the mortality ratio for men who never smoked regularly (by definition this ratio for men who never smoked regularly is 1.00). The latter ratio is essentially the ratio which would have been obtained if men who had never smoked regularly had been used as a control group; but this method of calculation provides somewhat more stable figures.

The pattern of relationships between smoking habits and death rates was found to be essentially the same for asbestos workers as for other groups of men as previously reported by numerous different investigations.

The following applies to deaths from all causes combined; and the mortality ratios relative to NSR (never smoked regularly) (see TABLE 6B). The mortality ratios were 1.98 for men who currently smoked 20+ cigarettes a day, 1.89 for those who currently smoked <20 cigarettes a day, 1.29 for pipe and cigar smoking, and 1.00 for men who never smoked regularly. The mortality ratio for ex-cigarette smokers who previously smoked 20+ cigarettes a day and had given up the habit <5 years was 2.03. This is higher than the mortality ratio for men who currently smoked 20+ cigarettes a day. It is a usual finding and is almost certainly due to the fact that men with incurable lung cancer or other advanced disease often give up smoking a few months or longer before they die. The 20+ a day cigarette smokers who had given up the habit for 5 to 9 years had a mortality ratio of 1.48 and those who had quit for 10+ years had a mortality ratio of 1.38, so their death rates were lower than the death rates of men who currently smoked 20+ cigarettes a day. The mortality ratios for ex-cigarette smokers who had previously smoked <20 cigarettes a day were; 1.85 (quit <5 years), 1.46 (quit 5 to 9 years), and 1.20 (quit 10+ years) as contrasted with a mortality ratio of 1.89 for men who currently smoked <20 cigarettes a day.

For lung cancer, the pattern of relationship was about the same as described above, but the mortality ratios of cigarette smokers were far higher. For example, the mortality ratio was 10.40 for men who currently smoked 20+ cigarettes a day and 9.15 for men who currently smoked <20 cigarettes a day.

There were too few deaths from each of various other diseases to present such a detailed analysis in relation to smoking habits. Some of the findings are briefly described below using the ratio Observed/Expected.

Only five men who never smoked regularly died of noninfectious pulmonary diseases whereas 17.1 deaths were expected in this group (ratio .29). These five died of asbestosis. Thus, for the subcategory asbestosis, there were five deaths among men who never smoked regularly whereas 13.3 were expected (ratio .38). Since all of the other men were smokers (mainly cigarette smokers) it follows that death rates from asbestosis were far higher in cigarette smokers than in nonsmokers.

The asbestosis death rates of men who currently smoked 20+ cigarettes a day was 2.8 times as high as the asbestosis death rate of men who never smoked regularly. It is clear that cigarette smoking greatly increases the risk of an asbestos worker dying

from asbestosis or asbestosis combined with pulmonary fibrosis and emphysema resulting from cigarette smoking.

None of the men who had never smoked regularly died of cancer of the esophagus, larynx, pharynx or buccal cavity. The expected number of deaths from these cancers was 3.6 for men who never smoked regularly. This suggests that in the absence of exposure to tobacco, exposure to asbestos dust may have little or no influence on death rates from such cancers.

For pleural mesothelioma, there were three observed deaths vs. 4.8 expected deaths among men who never smoked regularly (ratio .63); and five observed deaths vs. 3.2 expected deaths for pipe/cigar smokers (ratio 1.59). Thus, for men who never smoked cigarettes regularly there were eight observed deaths and eight expected deaths from this disease; so it appears that cigarette smoking has little or no effect upon death rates from pleural mesothelioma.

OTHER COMPARISONS

In TABLE 7A, the observed number of lung cancer deaths among asbestos workers in each of several different smoking categories is contrasted with the number expected if their age-specific lung cancer death rates had been the same as those for control group subjects who never smoked regularly. The observed numbers are based upon death certificate information. The table is confined to asbestos workers whose smoking habits were known.

Altogether, according to the death certificates, 276 lung cancer deaths occurred among the asbestos workers whose smoking habits were known, whereas only 6.0 were expected had their age-specific lung cancer death rates been the same as those for control group subjects who never smoked regularly. Thus, the mortality difference was 270.0 and the mortality ratio was 46.23.

The mortality ratios for various smoking categories were 87.36 for asbestos workers who currently smoked 20+ cigarettes a day; 50.82 for those who currently smoked <20 cigarettes a day; 36.56 for ex-cigarette smokers; 7.02 for pipe/cigar smokers; and 5.33 for asbestos workers who never smoked regularly.

Taken at face value it would appear that the risk of dying of lung cancer is about five times as great for a nonsmoker occupationally exposed to asbestos dust as for a nonsmoker without such exposure. However, because of small numbers the ratio is subject to considerable statistical sampling variation. By chance, the observed number might have been as low as one or two or as high as about nine. Therefore, all we can say is that the actual mortality ratio is probably >1.00 but could be as high as 12.00 or even a little higher. In any event, the mortality ratio for men who never smoked regularly was very small as compared with the mortality ratios of the cigarette smokers.

The mortality differences shown in TABLE 7B are copied directly from TABLE 7A. Altogether, 270.0 more of the asbestos workers died of lung cancer than would have died had their lung cancer death rates been the same as for nonsmokers not exposed to asbestos dust. These may be called "extra" lung cancer deaths. Of these "extra" deaths, 55.7% occurred in asbestos workers who currently smoked 20+ cigarettes a day; 11.3% in those who currently smoked <20 cigarettes a day; 29.9% in ex-cigarette smokers; 1.3% in pipe/cigar smokers; and 1.2% in asbestos workers who never smoked regularly. These figures are shown to give some idea of the degree to which the lung cancer death rate of a group of asbestos workers depends upon their distribution in regard to smoking habits.

TABLE 7A

OBSERVED NUMBER OF LUNG CANCER DEATHS OCCURRING 20+ YEARS AFTER ONSET OF OCCUPATIONAL EXPOSURE TO ASBESTOS DUST BY SMOKING HISTORY COMPARED WITH EXPECTED NUMBER BASED ON LUNG CANCER DEATH RATES OF CONTROL GROUP SUBJECTS WHO NEVER SMOKED REGULARLY

	Lung Cancer (DC)*			
Smoking History	Observed	Expected	Mortality Differences	Ratio Observed/ Expected
Total (with smoking habits known)	276	6.0	+270.0	46.23
History of cigarettes†	268	4.7	+263.3	57.63
Current 20+ cigarettes/day	152	1.7	+150.3	87.36
Current <20 cigarettes/day	31	0.6	+30.4	50.82
Ex-cigarettes	83	2.3	+80.7	36.56
Pipe/cigar only	4	0.6	+3.4	7.02
Never smoked regularly	4	0.7	+3.3	5.33

TABLE 7B

DISTRIBUTION OF LUNG CANCER MORTALITY DIFFERENCES PRESENTED IN TABLE 7A BY SMOKING HISTORY

	Lung Cancer (DC)*	
Smoking History	Mortality Differences	Percent of Total
Total (with smoking habits known)	+270.0	100.0
History of cigarettes†	+263.3	97.5
Current 20+ cigarettes/day	+150.3	55.7
Current <20 cigarettes/day	+30.4	11.3
Ex-cigarettes	+80.7	29.9
Pipe/cigar only	+3.4	1.3
Never smoked regularly	+3.3	1.2

*Died of lung cancer according to death certificate information.

†Includes the current cigarette smoking asbestos workers who did not specify the number smoked per day.

TABLE 8 differs from all of the other tables in that it shows lung cancer death rates per 100,000 man–years standardized for age on the age distribution of all of the asbestos workers in this study. The lung cancer deaths were so reported on death certificates. Just four groups are shown identified by occupational exposure to asbestos dust, (yes or no) and history of cigarette smoking (yes or no). The word "no" under the "history of cigarette smoking?" means never smoked regularly (pipe and/or cigar only smokers being excluded from this table).

The mortality differences shown here were calculated by subtracting the death rate of the "no, no" group from the death rate of each of the four groups. The mortality ratios were calculated by dividing the death rate of each group by the death rate of the "no, no" group.

The mortality ratios are 1.00 for "no, no," (asbestos no; cigarette smoking, no); 5.17 for "yes, no" (asbestos, yes; cigarette smoking, no); 10.85 for "no, yes" (asbestos, no; cigarette smoking, yes); and 53.24 for "yes, yes" (asbestos, yes; cigarette smoking, yes).

Now, suppose that occupational exposure to asbestos dust and cigarette smoking acted independently in respect to the production of lung cancer. In that event, the lung cancer death rate of asbestos workers with a history of cigarette smoking should be very close to the sum of the following three numbers: 11.3 (the rate for the "no, no" group), 47.1 (the mortality difference for the "yes, no" group), and 111.3 (the mortality difference for the "no, yes" group). The sum comes to 169.7 lung cancer deaths per 100,000 man–years which is a reasonable estimate of what the lung cancer death rate of the asbestos workers with a history of cigarette smoking would have been if there had been no synergistic effect of the combined exposure. In contrast, the observed lung cancer death rate of the "yes, yes" group was 601.6 per 100,000 man–years. The difference, (601.6 − 169.7) = 431.9 lung cancer deaths per 100,000 man–years, was presumably due to a synergistic effect in men with both of the two types of exposure (asbestos dust and cigarette smoking).

These particular figures apply to the particular group of asbestos workers included in this study. The net synergistic effect would not have been the same if their smoking habits had been different; and it probably would not have been the same if their lapsed times from first exposure to asbestos dust had been different or if the amount of asbestos dust they inhaled had been different.

TABLE 8

AGE-STANDARDIZED LUNG CANCER DEATH RATES* FOR CIGARETTE SMOKING AND/OR OCCUPATIONAL EXPOSURE TO ASBESTOS DUST COMPARED WITH NO SMOKING AND NO OCCUPATIONAL EXPOSURE TO ASBESTOS DUST

Group	Exposure to Asbestos?	History Cigarette Smoking?	Death Rate	Mortality Difference	Mortality Ratio
Control	No	No	11.3	0.0	1.00
Asbestos workers	Yes	No	58.4	+47.1	5.17
Control	No	Yes	122.6	+111.3	10.85
Asbestos workers	Yes	Yes	601.6	+590.3	53.24

*Rate per 100,000 man–years standardized for age on the distribution of the man–years of all the asbestos workers. Number of lung cancer deaths based on death certificate information.

COMMENTS

Underlying cause of death cannot always be ascertained with certainty; when cancer is clearly the cause of death, the primary site of the disease cannot always be ascertained with accuracy; and even when histologic sections are available, different pathologists may disagree on the histologic type of a cancer. These difficulties are troublesome from the standpoint of scientific accuracy as to details, but they make little difference to the workers and their families. For example, both peritoneal mesothelioma and cancer of the pancreas are painful diseases and the degree of pain is not dependent upon ascertaining which of these caused the death of the patient. If inadequate information results in error as to which of these two cancers caused death,

then it only means that the degree of association between death rates and exposure to asbestos dust is overestimated for one of the two diseases and correspondingly underestimated for the other.

It is true that some diseases are more painful than others and some are more expensive than others. But what is of most importance to the worker and most important to society is whether a particular type of occupational exposure leads to premature death or often leads to long term disability. Occupational exposure to asbestos dust results in both of these. This is sufficient reason to take strong preventive measures regardless of further details which are of scientific interest or which can have an influence on the outcome of a law suit.

Evidence from this study indicates a strong synergistic effect between two types of exposure (asbestos dust and cigarette smoking) in respect to risk of lung cancer.

Evidence from this study indicates that among asbestos workers, ex–cigarette smokers have substantially lower death rates than cigarette smokers who do not give up the habit. This should be brought forcefully to the attention of present asbestos workers. A young person who is so strongly addicted to cigarette smoking that he cannot break the habit or is unwilling to do so would be particularly well advised not to enter a trade involving exposure to asbestos dust.

Cigarette smoking increases the risk of death from asbestosis, providing another reason why asbestos workers should avoid that habit.

The major specific fatal effects of occupational exposure to asbestos dust are increased death rates from lung cancer, mesothelioma and asbestosis. The evidence indicates that occupational exposure to asbestos dust increases death rates from cancer of the colon–rectum, and cancer of the esophagus. It probably increases death rates from cancer of the kidney and from another set of cancers taken as a group (i.e., larynx, pharynx and buccal cavity). Aside from this, the evidence suggests that death rates from cancer of several other sites may be somewhat increased by occupational exposure to asbestos dust. Because of small numbers, we cannot identify which, if any, other specific sites are involved. As will be published in the near future by another group of investigators, asbestos bodies have been found in many different organs of asbestos workers who died and whose lungs were found to contain a very large number of asbestos bodies.[10]

It must be emphasized that only one group of asbestos workers is included in this investigation, namely members of the insulation workers union. We have indicated the degree of confidence we have in various specific findings, and in many instances we have given more than one estimate. For example, we said that "the mortality ratios for colon–rectum cancer ranged from 1.59 to 1.81," the mortality ratios having been calculated from each of four different sets of figures. In this particular case, all four sets of comparisons led us to the conclusion that death rates from colon–rectum cancer are increased by exposure to asbestos dust; but it would be folly to suppose that we have precisely determined the degree of association even in this group of asbestos workers.

Aside from this, the degree of association between exposure to asbestos dust and death rates from all causes combined as well as death rates from lung cancer vary with smoking history, lapsed time from onset of exposure to asbestos dust,[11] presumably with amount of asbestos dust inhaled, and probably with other factors as well. It seems very unlikely that any two identifiable groups of people with occupational exposure to asbestos dust are exactly alike in respect to all of the factors just mentioned. Therefore, we would not expect the exact figures reported here to be duplicated in a study of any other group of asbestos workers. We would expect the findings to be qualitatively the same but not quantatively identical.

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COMBINED EFFECT OF ASBESTOS EXPOSURE AND TOBACCO SMOKING ON FINNISH ANTHOPHYLLITE MINERS AND MILLERS

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The first health hazard to be noticed in asbestos workers was lung fibrosis. Much later, lung cancer and diffuse mesothelioma, in addition to some other malignancies, became the focus of medical interest. Initially, the lung cancer was thought to be caused solely by exposure to asbestos, but it is now evident that, even among asbestos workers, asbestos dust plays a relatively small role compared with tobacco smoking.

A previous report on this series of cases was published in 1974.[1] It was based on an analysis of the morbidity and mortality among workers employed at two anthyphyllite asbestos quarries in Finland. This earlier study showed that, compared with nonsmokers not exposed to asbestos, the relative risks of lung cancer were: for a nonsmoking asbestos worker, 1.4; for a smoker not exposed to asbestos, 12; and for an asbestos worker who smoked, 17.

A weak point in our study was that we could not obtain any direct information on the smoking habits of deceased asbestos workers. Now, 10 years later, the study has been supplemented with a more reliable estimate of the role played by smoking habits. In addition, the number of deaths among workers has increased in 10 years.

MATERIALS AND METHODS

Two anthophyllite asbestos quarries have been worked in Finland: one during 1918–72 and one from 1940 to 1944. They were owned by the same company and located within 10 km of each other. The annual output was about 15,000 metric tons. The asbestos was then ground in a hammer mill and fractioned according to fiber length. The workers were recruited mainly from the farming population living in this area. The quarries were located in a sparsely populated area with forests and lakes 50 km from the nearest city.

A fairly complete personnel register was kept by the company in the form of salary lists from 1936. The register contained names, birth dates, working periods, and roughly the kind of work done.

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